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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/12/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/695,919	GERL ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4 and 6-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment filed on April 21, 2003 has been received, entered into record and considered. The following information provided in the amendment affects the instant application:

1. Claim 5 is cancelled.
2. Claims 6-14 are added to the instant application.
3. Claim 1 is amended.
3. Remarks drawn to the rejections of claims 1-4 under 35 U.S.C. § 112, 102 (b) and 103 (a).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, 6-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, step (c), "adding a tracer to mixture" is vague and indefinite. It is unclear what tracer applicant refers to, i.e. human insulin or C-peptide standard. It is also not clear as to the function of this tracer. The relationship of this tracer to the other reagents in the method is not clearly set forth.

With respect to claim 1, step (e), "adding a C-peptide second antibody bead having at least one label to mixture" is vague and indefinite. It is unclear what this second antibody is specific for, i.e. C-peptide impurities or the first antibody.

With respect to claim 1, step (f), "detecting or determining the presence of the C-peptide-containing impurities", is vague and indefinite. It is not clear the detection refers to step (d), the antibody specific for the C-peptide impurities, or step (e), the C-peptide second antibody bead having at least one label to the mixture (d).

With respect to claim 6, line 2, "model compound" is vague and indefinite. It is unclear what "model' applicant refers to.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1-3, 6-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iizuka et al. (Biomedical Research (1990) 11: 417-423) in view of Hara et al.(EP 0484961) and Newgard (US 5811266).

Iizuka et al. teach measuring human C-peptide containing sample by mixing the sample with a first antibody specifically recognizing the C-peptide, and a tracer, e.g. radioiodinated I^{125} C-peptide, and a second antibody bead recognizing the first anti-C-peptide for determining the human C-peptide which is a degradation product from processing proinsulin. (See Abstract, Introduction, Materials and Methods).

However, Iizuka et al. do not teach (1) using recombinant human insulin as the sample, (2) non-radioactive assay to determine the C-peptide in a sample and (3) labeling the second antibody for detection. Newgard teaches using genetic recombinant method to produce human insulin. (Claim 1) Hara et al. teach using non-radioactive, i.e. fluorescent method for determining C-peptide. (Claims 1-4) Hara et al. teach labeling on an antibody recognizing the antibody specific for the C-peptide for an efficient assay. *Supra*. The instant recited acridinium ester moiety for tracer in claim 9, is a kind of fluorescent substances encompassed by Hara et al. reference. (page 2, line 52-54) Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided the assay of Iizuka et al. with the the genetic engineering method to produce human insulin as taught by Newgard, and non-radioactive substitute, i.e. fluorescence, and labeling another antibody recognizing the first antibody specific for the C-peptide as taught by Hara et al. since there is a great demand of human insulin and its quality control in diabetes research (See Newgard, Col 3, line 20-45), and the fluorescence labeling is an ideal substitute in the art and labeling on the second antibody for a better detection is a common practice.

With respect to claims 3 and 10, the instant claims recite buffer pH and the concentration of human insulin at certain ranges. It would have been obvious to one having ordinary skill in the art at the time the invention was made to optimize the assay with respect to different factors, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

With respect to claim 6, both references of Iizuka and Hara teach using antibody recognizing human insulin C-peptide for assay. Absence of clear evidence, "human insulin C-peptide" encompasses the "Lys(B3)-Glu(B29)-human insulin C-peptide."

With respect to claim 12, the instant claim recites using sheep to make antibody. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use different mammals to generate antibody since the human C-peptide is available and the isolation of antibody technique is well-known in the art.

5. Claims 4 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iizuka et al. Hara et al. as applied to claims 1-3, 6-12 and 14 above, further in view of Naithani et al.. (Fed. Rep. Ger. International Congress Series (1979) 468: 94-98)

Iizuka and Hara et al. references have been discussed but do not disclose antibodies specifically recognizing monkey C-peptide. Naithani et al. teach syntheses of *monkey* C-peptide and its derivatives. (See abstract) It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the conventional antibody technique to generate antibody specific for monkey C-peptide because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonal antibodies against it is *prima facie* obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. APp. & Int. 1990).

Allowable Subject Matter

6. Claims 7 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

7. The following is an examiner's statement of reasons for allowance: no prior art teaches or suggests using an antibody specific for C-peptide impurities recognizing both C-peptide and preproinsulin with nearly the same affinity.

Response to Applicant's arguments

8. Applicant's arguments with respect to claims 1-4 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9434 for regular communications and 703-746-9434 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641

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August 11, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
08/11/03